Complete Summary

GUIDELINE TITLE

Guideline for optimization of surgical pathological quality performance for radical prostatectomy in prostate cancer management: surgical and pathological guidelines.

BIBLIOGRAPHIC SOURCE(S)

Chin J, Srigley J, Mayhew LA, Rumble RB, Crossley C, Hunter A, Fleshner N, Bora B, McLeod R, McNair S, Langer B, Evans A, Expert Panel on Prostate Cancer Surgery and Pathology. Guideline for optimization of surgical and pathological quality performance for radical prostatectomy in prostate cancer management: surgical and pathological guidelines. Toronto (ON): Cancer Care Ontario (CCO); 2008 Sep 11. 81 p. (Evidence-based series; no. 17-3). [129 references]

GUIDELINE STATUS

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Prostate cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Oncology
Pathology
Surgery
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

Surgical Questions

To evaluate the recommended surgical procedures and outcomes for radical prostatectomy (RP), specifically:

1. What is the recommended extent of resection, and what is an acceptable positive margin rate?
2. What are the reported rates for surgical complications, specifically incontinence, erectile dysfunction, rectal injury, and blood transfusion, and does surgical technique (e.g., nerve sparing, bladder neck preservation) affect complication rates?
3. Under what circumstances should nerve-sparing techniques be used?
4. Which patients should receive pelvic lymph node dissection (PLND), and what is the recommended extent of PLND?

Pathological Questions

1. What are the recommended procedures for handling the RP specimen in the operating room and for handling and processing the RP specimen (with or without lymph nodes) in the pathology lab?
2. What diagnostic and prognostic elements should be included in the pathology report, what format should be used, and what reporting elements should be included?

TARGET POPULATION

Adult males with potentially curable prostate cancer for whom radical prostatectomy (RP) is the preferred treatment option

- Risk Categories: Patients may be considered "low", "intermediate", or "high" risk for treatment failure (e.g., local recurrence, biochemical failure with

prostate-specific antigen [PSA] relapse, emergence of metastatic disease) based on disease characteristics using the definitions

Patient Risk:

- Low Risk: PSA <10, Gleason ≤6, and clinical stage T1 or T2
- Intermediate Risk: PSA 10-20, and/or Gleason 7
- High Risk: PSA >20, Gleason ≥8, or clinical stage ≥T3

INTERVENTIONS AND PRACTICES CONSIDERED

1. Radical prostatectomy (RP)
2. Handling, processing and reporting of prostatectomy specimen
3. Pelvic lymph node dissection (PLND)

Note: This guideline does not deal with the choice of management options for prostatectomy. The assumption is that a detailed discussion with the patient regarding treatment options and various techniques for performing prostatectomy, appropriate to the given disease grade and stage, has already taken place. Neither salvage prostatectomy (following local radiotherapy failure) nor the role of neoadjuvant hormonal therapy in RP is addressed in this guideline.

MAJOR OUTCOMES CONSIDERED

- Positive surgical margin rates
- Recurrence rates
- Surgical complication rates

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search Strategy

The MEDLINE and EMBASE databases were searched for evidence related to the surgical questions during the month of March 2007, using the following text, MeSH, and EMBASE subject headings: 'prostatic neoplasms', 'prostate cancer', and 'prostate tumo?r'. These results were combined with the term 'prostatectom:' to provide a base pool of literature on surgical treatment of prostate cancer. These aggregate results were then combined with the terms 'nerve sparing', 'neurovascular bundles', 'nerve bundle', 'continence', 'incontinence', 'incontinent', 'urinary incontinence', 'pelvis lymphadenectomy', 'lymph node metastas?s', 'pelvis lymph node', 'lymph node dissection', 'pelvic lymph node dissection', 'pelvis surgery', 'lymph node excision', 'pelvic lymph node resection', 'lymph node resection', 'sentinel lymph node biopsy', 'neoplasm invasiveness', 'neoplasm residual', 'surgical margin$', 'margin status', 'surgical resection margin', 'margin clearance', and 'positive margin', with the total results being limited to human

studies in the English language published from 1996 through to March 2007. These searches produced 5,311 references.

In order to search for evidence-based reviews and clinical practice guidelines, the following text, MeSH, and EMBASE subject headings: 'prostatic neoplasms', 'prostate cancer', and 'prostate tumo?r' were used. These results were combined with the term 'prostatectom:' to provide a base pool of literature on surgical treatment of prostate cancer. These results were then limited to evidence-based reviews. A separate search of the Cochrane database was also conducted, using the term "prostatectomy."

Study Selection Criteria

Inclusion Criteria

Studies were considered eligible for inclusion if they were:

1. Randomized trials comparing radical prostatectomy (RP) with any other treatment
2. Prospective case series studies of RP
3. Retrospective review of RP patient reports
4. Studies with more than 100 subjects
5. Systematic reviews
6. Clinical practice guidelines
7. Studies concerning pelvic lymph node dissection (PLND) regardless of primary treatment
8. Database reviews

Exclusion Criteria

The following publication types were not eligible for inclusion in this report:

1. Review papers that were not systematic reviews
2. Letters to the editor
3. Single-patient case reports
4. Studies in which prostatectomy was salvage treatment
5. Studies that reported on cadavers or human tissue samples only
6. Studies that combined prostatectomy with other procedures (e.g., cystoprostatectomy)
7. Studies with less than 100 subjects
8. Studies concerning robotic surgery and techniques

NUMBER OF SOURCE DOCUMENTS

84 articles were included

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Due to the anticipated noncomparative sources of evidence in this report, no pooling was planned.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Formal consensus methods were not employed in the development of this guideline. Ontario urologists and pathologists were consulted in October 2007, prior to the completion of the draft document, in order to obtain feedback on the recommendations drafted by the working group. The consultation included a survey, conducted by email, and an in-person meeting to discuss the draft recommendations along with current data regarding radical prostatectomy (RP) performance in Ontario. All Ontario urologists listed in the Canadian Medical Directory were sent surveys, except for retired and pediatric urologists (N=106). Thirty-three returned the survey, and 26 attended the meeting. Pathologists from each Local Health Integrated Network (LHIN) were identified through the Cancer Care Ontario (CCO) Pathology and Laboratory Medicine Program. Fifty-five pathologists were sent questionnaires, 11 returned surveys, and six attended the meeting. The questionnaire was sent by email or fax. The survey results and the opinions expressed at the in-person meeting are summarized in the Results section in the original guideline document following the review of the evidence from the literature for each question.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Report Approval Panel

Prior to the submission of this evidence-based series (EBS) draft report for external review, the report was reviewed and approved by the Program in Evidence-Based Care (PEBC) Report Approval Panel, which consists of two members, including an oncologist, with expertise in clinical and methodology issues. Key issues raised by the Report Approval Panel and responses are detailed in the original guideline document.

External Review by Ontario Clinicians

Following the review and discussion of Section 1: Recommendations and Section 2: Evidentiary Base of this EBS and review and approval of the report by the PEBC Report Approval Panel (both in the original guideline document), the Expert Panel on Prostate Cancer Surgery and Pathology circulated Sections 1 and 2 to external review participants in Ontario for review and feedback.

Methods

Feedback was obtained through a mailed survey of 113 external review participants in Ontario (60 urologists, 29 pathologists, 11 surgical leads, eight radiation oncologists, and five medical oncologists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a guideline. Written comments were invited. The survey was mailed out on May 28, 2008. Follow-up reminders were sent at four weeks (postcard) and six weeks (complete package mailed again). The Expert Panel on Prostate Cancer Surgery and Pathology reviewed the results of the survey.

This EBS report reflects the integration of feedback obtained through the external review process with final approval given by the Expert Panel on Prostate Cancer Surgery and Pathology and the Report Approval Panel of the PEBC.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The following recommendations are based on the expert opinion consensus of members of the Prostate Cancer Surgery and Pathology Expert Panel (For membership, please see Section 2: Appendix 5 in the original guideline document) and informed by evidence from case series studies located through a systematic review of the available clinical evidence. The pathological questions are largely addressed by the protocol for invasive carcinomas of the prostate gland developed by the College of American Pathologists (CAP) with an effective date of April 2007 (endorsed by Cancer Care Ontario [CCO] and the Expert Panel on Prostate Cancer Surgery and Pathology). The full protocol and checklist for radical prostatectomy (RP) are included in Section 2: Appendix 1 in the original guideline document.

Surgical Recommendations

The main goals of radical prostatectomy (RP) are (a) complete eradication of the cancer-containing organ with negative surgical margins, (b) preservation of urinary function, and (c) preservation of erectile function, where appropriate, but, in some cases, it is not possible to achieve all three. Positive surgical margins are associated with higher rates of cancer recurrence, but techniques for the preservation of urinary and erectile function may result in positive margins.

The consensus opinion of the expert panel is that the following techniques and objectives form the basis for good surgical management during RP. In Ontario currently, most RPs are performed via the open retropubic route, but other methods are acceptable.

Radical Prostatectomy

- RP should be offered to low-risk and intermediate-risk patients for whom surgery is the preferred option after full discussion with patient and taking into account patient preferences.
- The decision to offer surgery to high-risk patients should be made with careful consideration. High-risk patients should be offered a referral for radiation consultation or review at a Multidisciplinary Cancer Conference (MCC). The intent of the MCC is to ensure that all appropriate diagnostic tests, all suitable treatment options, and the most appropriate treatment recommendations are generated for each cancer patient and discussed prospectively with a multidisciplinary team with the knowledge and tools to provide a full array of surgical interventions, systemic and radiation treatments, and supportive and palliative care. The incidence of positive margins in this patient group is expected to be higher than in that for pT2 disease.
- Sparing of the neurovascular bundles should be considered the "standard approach" except for high-risk patients.
- In patients with otherwise low or intermediate risk, where there is an increased likelihood of positive margins, based on clinical evidence, or the likelihood of extracapsular tumour extension and risk categorization, wide excision of the neurovascular bundles would be warranted in order to avoid compromising cancer control.
- The panel consensus was that attaining a positive margin rate of <25% for pT2 disease should be an achievable goal.
- The panel consensus was that the goals are to achieve rates of <1% mortality, <1% for rectal injury and <10% for blood transfusion in non-anemic patients.

Pelvic Lymph Node Dissection (PLND)

- Standard PLND should be mandatory in high-risk patients and is recommended for the intermediate group. PLND is optional for low-risk patients. (Standard PLND should include all lymphatic tissue along the external iliac vein from the lymph node of Cloquet distally to the bifurcation of the common iliac vein proximally and includes all lymphatic tissue in the obturator fossa.)
- Evidence and opinions on the role of extended PLND in high-risk patients are divided. (An extended PLND entails the removal of lymph nodes medial and lateral to the internal iliac vessels up to and around the bifurcation of the common iliac artery, with the genitofemoral nerve as the lateral limit.)

Technical Considerations for Radical Prostatectomy

- For additional specific details concerning technical considerations for RP refer to Section 2: Appendix 4.a in the original guideline document).

Pathological Recommendations

Handling of the Radical Prostatectomy Specimen in the Operating Room

- Frozen section analysis of the radical prostatectomy specimen (RPS) for margin status is not recommended.
- For routine handling, the RPS should be fixed in 10% neutral buffered formalin or other appropriate fixative. The specimen should be put in an appropriately sized container with a minimum formalin/tissue ratio of 10:1 (i.e., 500 cc formalin for a 50 cc prostate).

Pathology Requisition Information

- The surgical specimen should be accompanied by an appropriate pathology requisition that includes demographic and other identifying information, relevant clinical data (e.g., serum prostate-specific antigen [PSA], digital rectal exam [DRE] findings [T1c versus T2], Gleason score on biopsy), and the history of neoadjuvant therapy (e.g., hormones).

Pathology Report

- The surgical pathology report should include the relevant diagnostic and prognostic information as outlined in the College of American Pathologists Cancer Protocol for Carcinomas of the Prostate Gland. Cancer Care Ontario has recommended as a minimum standard that all mandatory elements on the College of American Pathologists checklist (Section 2: Appendix 2 in the original guideline document) be included in the RPS pathology report.
- It is recommended that the diagnostic and prognostic factors be presented as a synopsis as opposed to a narrative or paragraph form. Data from Cancer Care Ontario indicates that synopses are more likely to be complete.

Technical Considerations for Handling and Processing the Radical Prostatectomy Specimen in the Pathology Laboratory

- For additional specific details concerning technical considerations for handling and processing, refer to Section 2: Appendix 4.b in the original guideline document).
- In the Pathology Laboratory, the RPS (with or without lymph nodes) is accessioned in the usual fashion.
- The RPS should be fixed in neutral buffered formalin (minimum 10:1 ratio) for a minimum of 18-24 hours prior to sectioning. A microwave-assisted technique may be used to reduce fixation time.
- The prostate gland should be weighed and measured in three dimensions; seminal vesicles should be measured; accompanying lymph node specimens should also be measured and a record made of the number and size of grossly identified nodes.

- The outer aspects of the RPS should be carefully inked to identify the surgical margins, prior to tissue banking.
- After appropriate fixation and inking, the distal apical segment is transected and then serially sectioned, perpendicular to the inked surface. An en face (shave) technique is to be discouraged at the apex, as this approach can result in false-positive margin interpretation.
- The basal (bladder neck) aspect is commonly doughnut shaped and irregular. It is transected from the main specimen and should also be submitted in a perpendicular fashion to minimize the possibility of a false-positive margin at this location.
- The intervening transverse sections can be either totally or subtotally submitted using regular-sized blocks. The submission protocol should be documented with an appropriate diagramatic or written block legend.
- For subtotal submissions, a systematic approach to include the posterolateral peripheral zone should be used.
- All lymph nodes accompanying the RPS should be submitted for histological analysis. It is not necessary to submit all perinodal fat, although it is often difficult to distinguish between adipose tissue and fatty lymph nodes.
- The full College of American Pathologists checklist and protocol for RP are included in Section 2: Appendix 1 of the original guideline document.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by retrospective reviews, databases, case series, and non-randomized prospective studies, often without comparison groups.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate surgical and pathological management of prostate cancer resulting in complete eradication of the cancer-containing organ, with negative surgical margins, preservation of urinary function, and preservation of erectile function where appropriate

POTENTIAL HARMS

Surgical complications of radical prostatectomy

- Urinary incontinence
- Erectile dysfunction
- Rectal injury

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to nerve-sparing techniques include prostate-specific antigen (PSA) level, amount of high-risk cancer, extracapsular extension, and pathological stage.

QUALIFYING STATEMENTS

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Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Chin J, Srigley J, Mayhew LA, Rumble RB, Crossley C, Hunter A, Fleshner N, Bora B, McLeod R, McNair S, Langer B, Evans A, Expert Panel on Prostate Cancer Surgery and Pathology. Guideline for optimization of surgical and pathological quality performance for radical prostatectomy in prostate cancer management: surgical and pathological guidelines. Toronto (ON): Cancer Care Ontario (CCO); 2008 Sep 11. 81 p. (Evidence-based series; no. 17-3). [129 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Sep 11

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Expert Panel on Prostate Cancer Surgery and Pathology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Expert Panel on Prostate Cancer Surgery and Pathology who were involved in the writing of this document were polled for potential conflicts of interest.

No conflicts were declared.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.
- A checklist for surgical pathology cancer case summary is included in the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI Institute on August 27, 2009.

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Date Modified: 11/30/2009